

Attorney Docket No.: **KBI-0003**
Inventors: **Ranganathan and Dickstein**
Serial No.: **09/557,011**
Filing Date: **April 20, 2000**
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The Examiner acknowledges that claim 1 recites a new limitation whereby the sorbents possess a gut clearance rate for urea of at least 5.6 ml./min. However, the Examiner suggests that this limitation is merely an extrinsic property which does not materially change the composition. The Examiner suggests that because each respective sorbent inherently possessed specific absorption affinities for uremic toxins as displayed in the prior art, it would have been expected that a combination of sorbents would have had an additive effect with regard to absorption rates. Further, the Examiner states that this is a CPA of the earlier application no. 09/557,011 and all claims are drawn to the same invention claimed in the earlier application and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the earlier application, and hence the Examiner has issued a first and final Office Action in this case. Applicants respectfully disagree with the Examiner's issuance of a final action in this case.

In the previous office action, the Examiner issued an Advisory Action stating that the new limitation to the claims which recites "wherein the sorbents possess a gut clearance rate for urea of at least 5.6 ml./min" was not considered previously on the merits and that new consideration as well as a new search would be necessary on the amended claims. Hence, the new limitation was not entered and a CPA was pursued by the Applicants. Now in the first Office Action in the CPA the Examiner has suggested that the scope of the claims has not changed and that the new limitation properties were inherent in the composition. The Examiner has argued inapposite positions with relation the new limitation. Applicants respectfully submit that they should have received a Non-final

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Action in this case because they filed an Amendment which materially changed the claims and which was not entered due to the Examiner indicating in an Advisory Action that a new search was required. If the new limitation was truly inherent, an Advisory Action necessitating a new search should not have been issued in the previous case, but rather the Applicants should have been informed that the previous rejections would not be avoided by the amendment, as exemplified in MPEP 714.13.

However, in an earnest effort to facilitate prosecution in this case, claim 1 has been further amended to clarify and distinguish the present invention. Specifically, it is recited that the composition of the present invention is both microencapsulated and enteric coated as supported throughout the specification and at page 9, lines 20-25.

Yatzidis et al. teach the use of locust bean gum as an oral sorbant. Yatzidis et al. do not teach either a microencapsulated or an enteric coated composition.

Prakash et al. teach microencapsulated *genetically engineered E.coli* cells containing the *Klebsiella aerogens urease* gene for urea removal. Prakash et al. teach against oxystarch use due to high dose requirements, and low *in vivo* urea removal. Prakash et al. do not teach a combined microencapsulated and enteric coated composition.

Goldenhersh et al. teach that adsorption competition interferes with the adsorption of creatine on activated carbon. Goldenhersh et al. teach that microencapsulation of activated carbon with the polymers is not taught as useful to recover significant amounts of uric acid. See column 1, page 253. Goldenhersh et al. do not teach the combination of the carbon or

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other sorbents with a bacterium. Goldenhersh et al. do not teach a combined microencapsulated and enteric coated composition.

MPEP § 2143 is quite clear; to establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art to modify the reference or combine the reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art references when combined must teach or suggest all the claim limitations. The cited prior art combination fails to meet these basic criteria.

The composition of the instant invention alleviates the symptoms of uremia using a microencapsulated and enteric coated mixture of: (1) sorbents with specific adsorption affinities for uremic toxins wherein the sorbents possess a gut clearance rate for urea of at least 5.6 ml/minute; and (2) a bacterial source which metabolizes urea and ammonia.

None of the references provide any teaching or suggestion of coupling a bacterium with sorbents in a microencapsulated and enteric coating to treat uremia. Thus, the combination of references fails to teach or suggest all of the claim 1 limitations.

As the basic criteria set forth for establishing a *prima facie* case of obviousness are not met by the cited references, this combination of prior art cannot render obvious the instant claimed invention.

Withdrawal of this rejection under 35 U.S.C. § 103(a) is therefore respectfully requested.

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Conclusion

Applicants believe that the foregoing comprises a full and complete response to the Office Action of record. Accordingly, favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "**Version with Markings to Show Changes Made**".

Respectfully submitted,



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Version with Markings to Show Changes Made

In the claims:

Claim 1 has been amended as follows:

1. (Amended) A microencapsulated and or enteric coated composition comprising:

- (a) a mixture of sorbents with specific adsorption affinities for uremic toxins wherein the sorbents possess a gut clearance rate for urea of at least 5.6 ml/minute; and
- (b) a bacterial source which metabolizes urea and ammonia.